International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.3, No.4, pp 1769-1780, Oct-Dec 2011

Spectrophotometric determination of drugs using 2,3 Dichloro 5,6 dicyano *P*-Benzoquinone as Analytical reagent

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Abstract: Seven drugs *viz.,* Paroxetine, Famotidine, Quetiapine, Dextromethorphan, Levofloaxacin, Irbesartan and Itraconazole were tested for the formation of charge transfer complexes with DDQ and the interaction formed a basis for spectrophotometric determination of the drugs. Acetonitrile was found to be suitable solvent for the analysis. The methods have been validated in terms of ICH guidelines The complexes were found to have 1:1 composition and have stability of the order 10^{3} to 10^{4}
Key words: Spectrophotometry, DDQ, Drugs, Quantification, Validation.

INTRODUCTION

2,3-Dichloro 5,6- dicyano- *p*-benzoquinone(DDQ) is an oxidizing[1], dehydrating agent[2] in synthetic organic chemistry as well as it is known for its interaction with drugs having donor sites in their structures, and form ion-pair charge transfer complexes which offers a basis for quantification of the drugs[3-6].

Thorough survey of literature on the following drugs revealed that quantification using DDQ as analytical reagent has not been reported yet although the reagent is common, known to offer simple, sensitive method of quantification for drugs. This prompted the authors to develop quantification methods for the following drugs, (Scheme 1), using DDQ as a chromogen and hence tested them for the formation of charge transfer complexes which is expected to form a basis for the quantification of the drugs The physiological activity of the drugs and methods so far used for their quantification are:

Paroxetine (PXT), is (3S, 4R)-3-[(1,3-Benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl) piperidine hydrochloride . It is a new generation antidepressant drug. It is comparable to the tricyclic antidepressants in their clinical efficacy, however, but is safer. It is also used in the treatment of obsessive compulsive disorder, panic fits, generalized anxiety disorders and social phobithe Recently reported quantification method[7] depends on the reaction of the drug with 2,4-Dinitrofluorobenzene, wherein other quantification methods are cited .

Famotidine (FMD), chemically 3-[[[(2-aminoiminomethyl)amino-]4-thiazolyl]methyl]thio]-N-(amino sulfonyl) propaninidamide, is used in the treatment of duodenal ulcer, gastric ulcer, stress ulcers and gastritis Its quantification is reported by Chakravarthy *et al*[8] quoting earlier methods of determination.

Quetiapine fumarate (QTF) – chemically known as {2- (2-(4-dibenzo[b,f] [1,4]thiazepine-11-yl-1-piperazinyl)eth oxy)ethanol, fumaric acid – a dibenzothiazepine derivative is one of the most recent 'atypical' antipsychotic drugs It is a selective monoaminergic antagonist with high a. nity for the serotonin Type 2 (5HT2) and dopamine type 2 (D2) receptors. QTF is prescribed for the treatment of schizophrenia and other psychotic or schizoactive disorders . QTF was approved by the FDA for the treatment of Bipolar I (Bipolar II) disorder as a monotherapeutic agent. A recent method of quantification is published by Kanakapura Basavaiah [9] wherein other methods of quantification have been mentioned.

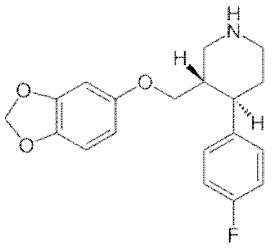
Dextromethorphan hydrobromide (DEX), [(+)-3-Methoxy-17-methyl-9á, 13á,14á-morphinan hydrobromide monohydrate] is a cough suppressant, used for the relief of non-productive cough; it has a central action on the cough centre in the medulla. A recent method of quantification is published in InternatIonal journal of Biomedical scIence[10] wherein the authors presented earlier studies on assay of the drug.

Levofloxacin (LFC) is a fluoroquinolone antibacterial agent. It is a secondgeneration members of quinolones and is greatly effective against both Gram-negative and Gram-positive bacteria that are resistant to other antibacterials. Levofloxacin, is used in the treatment of MDR tuberculosis. It is recently quantified by direct UV spectrophotometric method [11]. The report includes past quantification references on the drug.

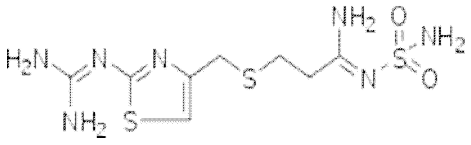
Irbesartan (IRB) is an angiotensin receptor antagonist1, and it is chemically 2-butyl -3[(29-(1H-tetrazol-5yl) [1, 19-biphenyl]-4-yl] methyl] 1, 3-diazaspirol [4, 4] non-1-en-4-one. Recent determination by UV method [12] is preceded by many methods cited therein.

Itraconazole (ITR), is (±)-2-sec-Butyl-4-[4-(4-{4- [(2R,4S)-2-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-4-ylmethoxy] phenyl}piperazin-1- yl)phenyl]-2,4-dihydro-1,2,4-triazol-3-one. It is an orally active triazole antimycotic agent, which is active against a broad spectrum of fungal species including, *Cryptococcus, Candida,* and *Aspergillus.* Its oral bioavailability was found to increase when taken with food, with plasma concentration approximately two times that taken in the fasting state. It is extensively metabolized in the liver, mainly via an oxidative pathway, into the bioactive metabolite hydroxyl itraconazole. Spectrofluorimetric Determination of Itraconazole in dosage forms and spiked human plasma is a recent reference [13] in which various earlier methods of quantification are reviewed.

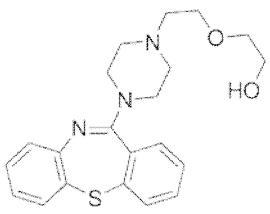
Scheme 1 - Structures of the drugs



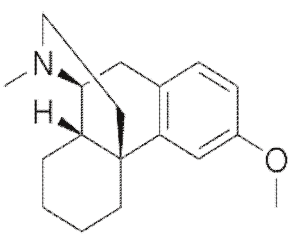
1 Paroxetine



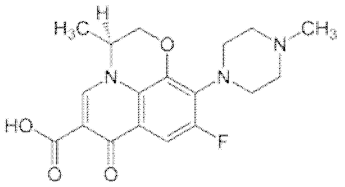
2 Famotidine



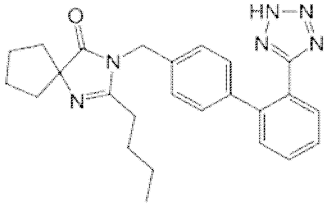
3 Quetiapine



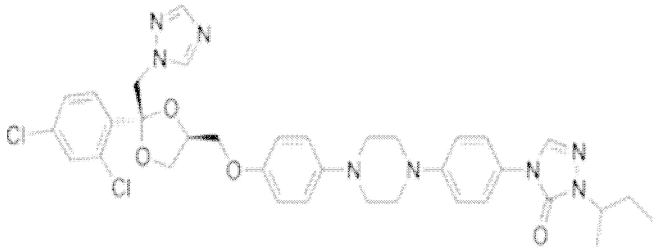
4 Dextromethorphan



5 Levoflaxacin



6 Irbesaartan



7 Itraconozole

EXPERIMENTAL

INSTRUMENT

The spectra of individual components and charge transfer complexes were recorded on Shimadzu 140 double beam spectrophotometer as well as on Thermo Nicolet 100 & Elico 159 UV- Visible single beam spectrophotometers using matched pair of Quartz cells of 10mm path length.

MATERIALS

2,3-Dichloro 5,6- dicyano- *p*-benzoquinone(DDQ) was obtained from Sd Fine Chem India Ltd.(mp 213-214^0 C). It was recrystallised twice from a 3:1 mixture of chloroform and benzene. A stock solution of 60mg/100ml w/v (2.6 x 10^{-3} *M*) in acetoniltrile was freshly prepared. . The drugs used in study are procured from Hetero drugs pvt.ltd. Hyderabad. Most of the drugs procured are in the form of their acid salts. They have been neutralized by adding calculated amount of NaOH/NH_4OH as required followed by extraction with ether or $CHCl_3$. They were recrystallized from suitable solvent till TLC pure.. Stock solutions of drugs are prepared first (1mg/ml) and are further diluted according to the requirement for their analysis.

The materials used are spectrograde acetonitrile, AR grade methanol, ether, NaOH and NH_4OH all of them are supplied by S D fine chemicals, Mumbai.

EXTRACTION OF DRUGS FROM PHARMACEUTICALS.

1 Paroxetine HCl

Ten tablets (Pexep-10mg) were weighed, powdered and an accurately weighed amount of powder equivalent to 50mg of paroxetine HCl was dissolved in 40ml of water followed by sonnication for 20minutes, then filtered into a volumetric flask. The residue was washed with a few millilitres of water and filtered , washings were added to the same flask. The paroxetine hydrochloride solution was taken in a separating funnel containing ether followed by the addition of 0.1 N sodium hydroxide. The contents are shaken well and allowed to stand for some time. Both the layers are separated. Extraction continued in two portions with 25ml of ether. Ethereal layer is separated and evaporated. To the content acetonitrile is added and further dilutions are done depending up on the requirement.

2. Famotidine

Twenty tablets (Autidine - 20mg) were weighed, and finely powdered. An accurately weighed quantity of the powdered tablet contents equivalent to 50mg of the active ingredient was transferred into a 100ml calibrated flask, and dissolved in about 100ml of methanol. The contents of the flask were swirled, sonicated for 5minutes. The mixture was mixed well, filtered and evaporated to dryness. Residue was

dissolved in acetonitrile heating on waterbath for the complete dissolution of drug. A measured volume of the prepared solution was diluted quantitatively to 100ml with acetonitrile, and the resulting solution was used for the analysis.

3. Quetiapine

For the analysis of pharmaceutical formulations 10 tablets (Q-Pin – 25mg) were weighed and pulverised. A weighed quantity of the powdered tablets equivalent to 50mg of quetiapine fumerate was transferred into a volumetric flask containing methanol. The content was filtered through Whatmann filter paper into a beaker. The content was washed with a few ml of methanol and washings were passed into the beaker. Methanol was then evaporated by heating on water bath and acetonitrile is added. From this solution aliquots volumes covering the working concentration range were transferred into 10ml volumetric flask and was determined.

4 Dextromethorphan

The contents of ten tablets (Lastuss-CT-10mg) were crushed, powdered, weighed out and the average weight of tablets were determined. An accurately weighed powdered tablets equivalent to 50mg of dextromethorphan HBr was dissolved in 20ml double distilled water with shaking for 5 minutes and then filtered. The dextromethorphan HBr solution was then taken in a separating funnel containing ether followed by the addition of 0.1N sodium hydroxide. The content of separating funnel were mixed well and shaken for 5 minutes. The two layers are separated. Ethereal layer is evaporated and the residue is dissolved in acetonitrile (in case of *p*-CA, TCNE & DDQ acceptors) or in 1,2 dichloroethane (in case of Iodine acceptor) for further dilutions.

5. Levofloxacin

Four tablets (Alevo-250mg) were powdered and an equivalent amount of 500mg of levofloxacin was added to about 100ml of methanol and sonicated it for 30 minutes to dissolve. Filtered it through Whatmann filter paper into a beaker and the residue was washed thoroughly for the complete recovery of the drug. Methanol was evaporated. To the content acetonitrile solvent is added and further dilutions are made as required with solvent for the determination of the drug.

6. Irbesartan

The powdered contents of two tablets (Irbest-150mg) of strength were weighed and grounded. The powder equivalent to 50mg irbesartan was stirred well with acetonitrile. The solution was filtered through Whatmann filter paper in a 100ml volumetric standard flask and the residue was washed well with acetonitrile for complete recovery of the drug. The content of the standard flask was then diluted with acetonitrile to get required concentration for the analysis of the drug. The amount of irbesartan was determined following the procedure.

7. Itraconazole

Two tablets (Candistat–100mg) were powdered and equivalent to about 200mg of itraconazole was added to about 100ml of methanol and filtered through Whatmann filter paper. The residue was washed thrice with methanol for complete recovery of drug and methanol was evaporated. To the content acetonitrile solvent is added. The aliquot portions of this stock solution were further diluted with solvent to get the final concentration required for the determination of the drug.

SPECTRA

The spectra of ion – pair Charge transfer complexes were recorded in CH_3CN for quantification studies as well as to evaluate other parameters like stability constants and stoichiometry of the complexes from absorption studies on characteristic absorption band of anion of the acceptor. The spectra of each sample at 2 or 3 different concentration have been recorded on scan mode and for the remaining optical density was noted on fixed mode.

RESULTS AND DISCUSSION

DDQ is a strong π- electron acceptor having electron affinity 1.9 eV which interacts instantaneously with the basic nitrogenous compounds to form charge transfer complexes of n – π type[15]. DDQ solution in acetonitrile displayed a maximum absorption peak at 350nm while all the drugs analysed in the present study showed a maximum absorption peak below 250 nm. Mixing the solutions of drug and the solution of DDQ in acetonitrile yields intense reddish brown color and causes an immediate change in the absorption spectrum with new peaks at 455, 545 and 588 nm (Fig. 1).

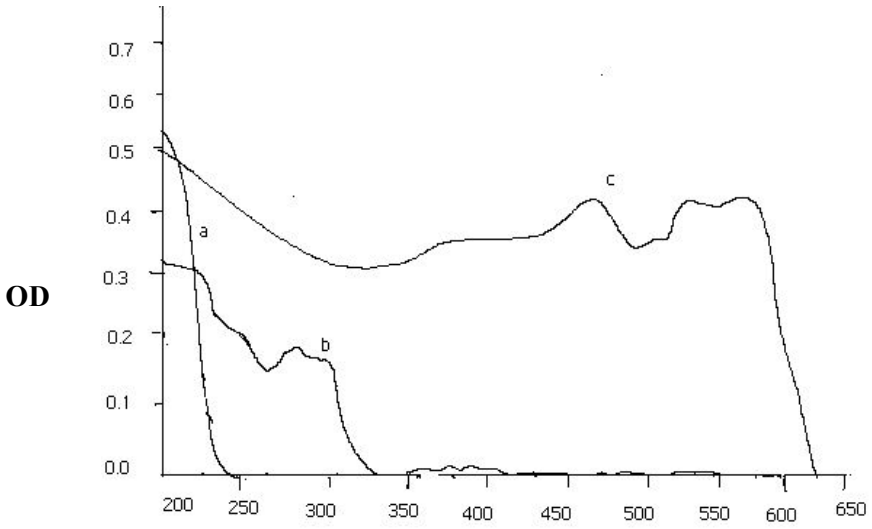
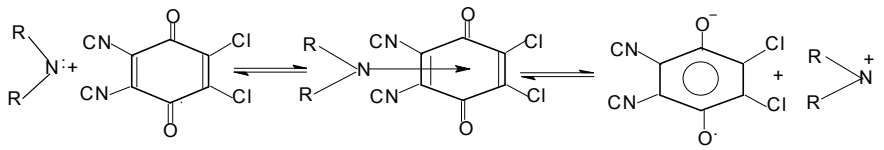


Fig. 1 Absorption spectra of a) pure drug b) DDQ in acetonitrile and c) its charge transfer complex with Dextromethorphan..

$$D + A \underset{\text{non-polar solvent}}{\rightleftharpoons} [D^{+}A^{-}] \underset{\text{polar solvent}}{\rightleftharpoons} D^{+} + A^{-}$$

Donor Acceptor Donor-Acceptor complex or charge transfer complex cation anion

The interaction of drug with DDQ at room temperature was found .
to yield a colored charge transfer complex. In polar solvents, complete electron transfer from drug as an electron donor (D), to acceptor moiety (A) takes place resulting in the formation of intensely colored radical anion of DDQ. The reaction sequence can be shown in Scheme 2.



Drug (Donor) Acceptor (DDQ) Donor-acceptor complex or Charge transfer complex anion cation

Scheme 2 .

PROCEDURE FOR CALIBRATION

Seven drugs are found to respond to DDQ in acetonitrile *viz.,* Paroxetine, Famotidine, Quetiapine, Dextromethorphan, Levofloxacin, Irbesartan and Itraconazole

Into a series of 10ml volumetric flasks, different volumes of standard solutions of drug were transferred. To each flask, 2ml of (2.6×10^{-3} *M*) DDQ solution in acetonitrile was added and remaining volume was made up by solvent. The absorbance of the solution was measured after 2 min. of mixing against blank at 455, 545, and 588nm.

Calibration curves **(**Fig.2) were linear for all the drugs whose limits are mentioned in (Table1). Slope , intercept, correlation coefficient of the calibration curves are calculated and tabulated.

Effect of concentration of acceptor

To establish the optimum concentration of reagent, Paroxetine 70 µg/ml, Famotidine 80 µg/ml, Quetiapine 140 µg/ml, Dextromethorphan 80 µg/ml, Levofloxacin 150 µg/ml, Ofloxacin 150µg/ml, Irbesartan 120 µg/ml, Itraconazole 640 µg/ml and were allowed to react with different volumes of *viz*., 0.4, 0.8, 1.2, 1.6, 2.0, 2.4ml of DDQ (2.6×10^{-3} *M*). The results showed that the highest absorbance was obtained with 1.8ml which remained unaffected by further addition of DDQ. Hence 2ml of the reagent was used for the determination of drugs (Fig. 3).

Table 1 Spectraland analytical parameters of ion pair complexes of DDQ with drugs

Parameter	**PXT**	**FMD**	**QTF**	**DEX**	**LVF**	**IRB**	**ITR**
λ_{max} (nm)	545	545	545	545	545	545	545
Beer's law limits (µgml^{-1})	5-70	4.3-83	10-140	4-76	5.6-154	13.4-121	24-640
Molar absorptivity (L mol^{-1} cm^{-1})	5211	3732	3397	3321	2555	1376	1202
Formation constant, K, M^{-1}	9000±60	4000±50	4000±60	3000±60	2500±70	800±50	800±70
Sandell sensitivity (µg cm^{-2})	0.063	0.090	0.112	0.0873	0.140	0.311	0.586
Slope b	0.0158	0.01109	0.008870	0.011454	0.00707	0.003213	0.001706
Intercept (a)	0.0635	0.04755	0.079823	0.032379	0.063772	0.017483	0.0522
Correlation coefficient	0.997351	0.997540	0.997421	0.9987150	0.99652	0.999141	0.998244
Standard deviation of intercepts (% n=5)	0.00485	0.002	0.0019	0.0036	0.0016	0.0013	0.0013
Limit of detection, µgml^{-1}	1.01	0.59	0.706	1.03	0.74	1.37	2.51
Limit of quantification µgml^{-1}	3.03	1.78	2.120	3.11	2.23	4.12	7.54
Reegression equation Y= bx+a	Y=0.0635 +0.0158x	Y=0.04755 +0.011x	Y=0.0798 +0.00887x	Y=0.0323 +0.01145x	Y=0.0637 +0.00708x	Y=0.0174 +0.0032x	Y=0.052 +0.0017x

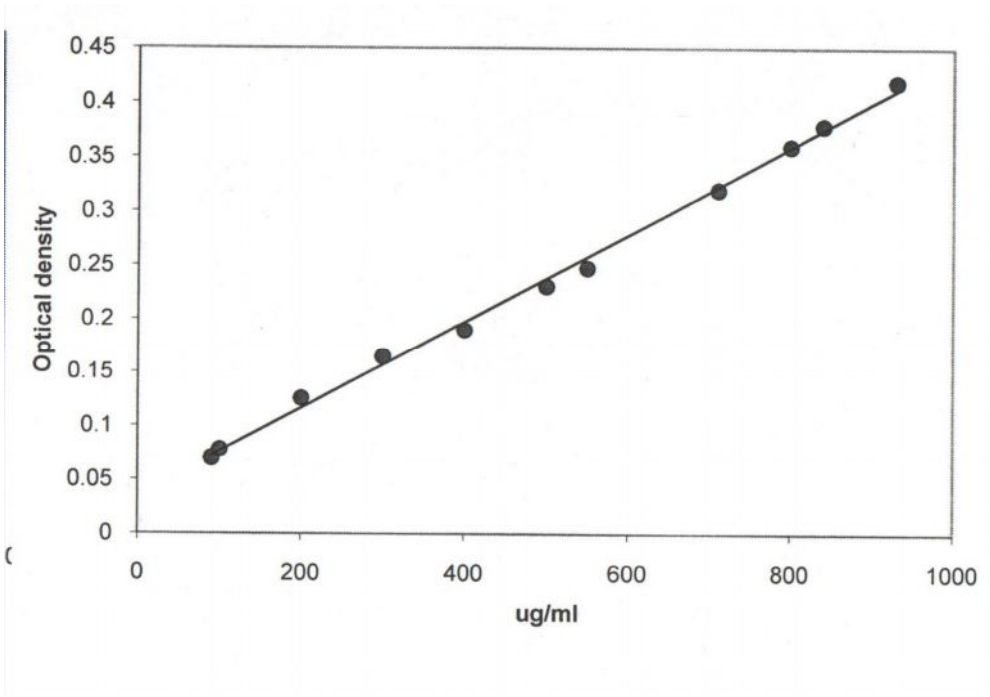


Fig.2 Calibration curve for quantification of irbesartan using DDQ as analytical reagent

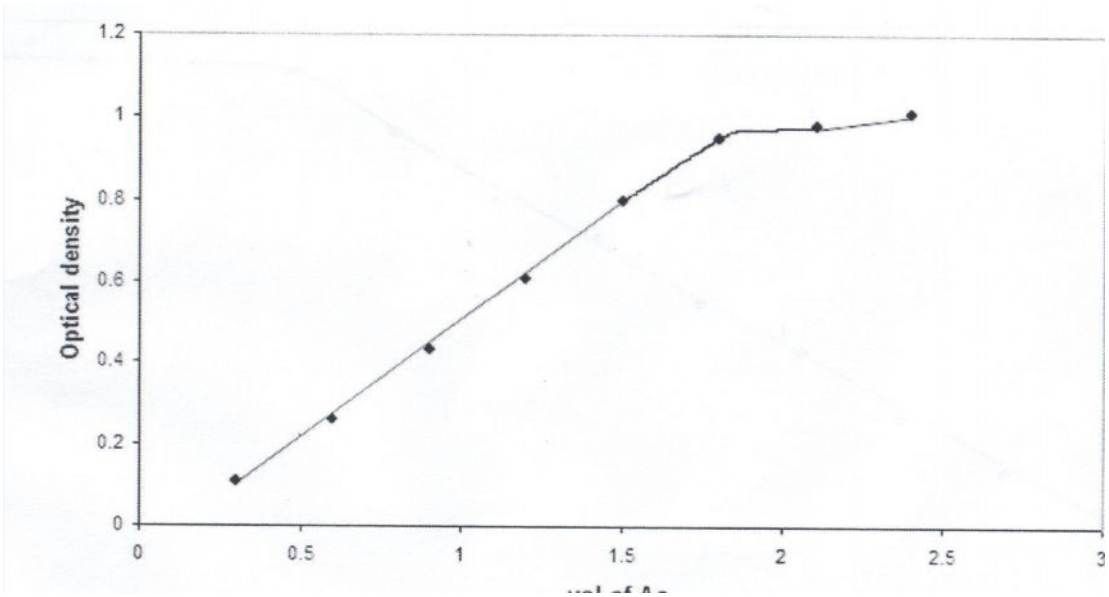


Fig 3 Effect of volume of reagent on the optical density of the Ion - pair complex of DDQ and Famotidine (80 μg ml^{-1})

Table 2 The effect of solvent on the Optical density of charge transfer band of DDQ with Quetiapine (80 μg/ml)

S.No	Solvent	Optical density
1	Acetonitrile	0.82
2	Methanol	0.76
3	1,2- dichloroethane	0.15
4	Chloroform	0.11
5	Carbon tetrachloride	0.07

Effect of concentration of drug

To a fixed volume of acceptor mentioned above , different volumes of drug of random concentration was added. Solutions developed coloration. Absorbance was measured at 455, 545, and 588nm. Beer's law was obeyed by these solutions to certain extent of concentration and above which linearity was not observed. This concentration is taken as optimum concentration and stock was prepared. The stock was further diluted to get at least 8 – 10 points in calibration curves range.

Similarly when the concentration is below certain limit, points scattered. This was taken roughly as a measure of limit of detection which is further confirmed by following the procedure for determination of LOD and LOQ.

Effect of reaction time

The interaction of DDQ with drugs resulted in the formation of colored product which stabilized within 2 min. of mixing. The developed color remained stable at room temperature for about an hour. After two hours many solutions turned brownish black and are opaque. After a day all solutions decolorized hence the measurements were made immediately after mixing the solutions.

Effect of Organic solvent:

Both polar and non-polar solvents such as chloroform, methanol, 1,2 dichloroethane, acetone and acetonitrile were used to select elegant solvent for the analysis of the drug. Acetonitrile is found to be suitable solvent as it produces maximum optical density with a fixed concentration of drug, while other solvents mentioned above are found to be unsuitable as they produced lower absorbances due to incomplete dissociation of complex. Hence acetonitrile is used throughout the study (Table 2).

VALIDATION OF THE PROPOSED METHODS

The methods developed have been validated in terms of guidelines of international conference of harminisation (ICH) [15] *viz.,* selectivity, sensitivity, precision , accuracy, linearity, LOD, LOQ Sandell's sensitivity and robustness. The methods are selective and can differentiate the analyte from the excipients.. The precision is tested by repeating each experiment at least 6 times while the accuracy has been tested by taking known weight of sample and performing recovery experiments. The values %RSD and t- and F tests are in the permissible range of experimental errors. (Table 3). Sandell's sensitivity "Milligrams of drug per liter required to produce a change in the absorbance by 0.001 absorbance units" have been calculated for all the drugs. Limit of Detection "The lowest amount of analyte in a sample that can be detected, but not necessarily quantitated as an exact value" and Limit of Quantification " The lowest amount of analyte in a sample that can be quantified using Calibration curves" have been calculated by using equations available in the literature.

$$LOD = 3.3s/S$$
$$LOQ = 10s/S.$$

Where s= standard deviation of the intercept (n = 5)
S = slope of Calibration plot

The robustness of the methods are examined by performing the experiments on three different spectrophotometers with excellent tally of absorbance values. The methods developed have also been applied for the analysis of pharmaceuticals. The recovery experiments performed show high accuracy and precision and the results are compared to the available validated reported methods on each drug. The values %RSD and t- and F tests are in the permissible range of experimental errors. (Table 4) and show that the methods can be used in both pharmaceutical and drug industries.

Table 3 Determination of accuracy and precision of the methods on pure drug samples

Drug	Taken (μg/ml)	Found (μg/ml)	Recovery (%)	RSD (%)	Proposed method Mean ± SD	Reference method Mean ± SD	t-test	F-test
PXT	20	19.91	99.58	1.77	99.95	98.4	0.75	2.04
	30	29.62	98.73	1.55	±0.94	±1.04	(2.45)	(9.01)
	40	40.41	101.04	1.31				
	50	49.19	98.39	1.69				
	60	58.20	97.00	2.06				
FMD	20	20.01	100.07	0.22	99.99	100	1.56	0.97
	40	40.00	100.02	0.15	±0.01	±0.012	(2.23)	(3.97)
	60	59.99	99.99	0.09				
	80	79.98	99.98	0.10				
	82	81.90	99.88	0.06				
QTF	20	19.8	100.52	0.89	100.30	100.66	0.65	1.04
	35	35.0	99.82	0.02	±0.59	± 0.53	(2.26)	(4.38)
	40	39.72	100.69	0.67				
	65	64.69	100.47	1.34				
	100	100.83	99.96	0.86				
DEX	30	30.60	107.1	2.07	100.13	100.26	2.22	1.92
	40	39.80	96.2	1.81	±0.08	± 0.07	(4.38)	(4.38)
	60	60.20	99.8	1.34				
	70	70.39	100.1	1.00				
	75	74.37	97.33	1.18				
LVF	25	25.27	101.10	1.62	99.96	100.38	0.80	1.71
	42	41.68	99.25	1.87	±0.71	±0.72	(2.45)	(9.01)
	60	60.00	100.00	0.15				
	80	79.39	99.24	0.63				
	130	130.3	100.23	0.76				
IRB	25	24.99	99.97	0.12	99.99	99.98	0.64	1.27
	30	30.01	100.05	0.11	±0.026	±0.023	(2.31)	(5.05)
	50	50.00	100.00	0.14				
	70	70.02	100.04	0.08				
	90	89.93	99.92	0.14				
ITR	30	30.03	100.3	0.36	99.80	99.40	0.93(2.31)	1.69(3.97)
	100	99.67	99.01	0.60	±0.76	±0.69		
	200	199.63	100.04	0.28				
	320	319.68	99.69	0.18				
	330	329.93	100.00	0.17				

STABILITY CONSTANTS OF ION – PAIR CHARGE TRANSFER COMPLEXES

In literature the author noticed that Benesi - Hildebrand method (BH)[14] is widely used for determination of stability constant *K* and molar absorption coefficient, ε.

Ao/ D = 1/ K (Do) ε +1/ ε

Above equation is known as BH equation and a plot of Ao/ d Vs 1/ Do is a straight line from whose slope and intercept the *K* and ε are determined. The BH method however demands the concentration of donor Do > > Ao (Do should be 20 to 100 times the acceptor concentration) and many times the correct separation of *K* and εis also doubtful.

Table 4Application of the proposed methods for the assay of drugs

Drug	Taken (μg/ml)	Found (μg/ml)	Recovery (%)	RSD (%)	Proposed method Mean ± SD	Reference method Mean ± SD	t-test	F-test
PXT	30 50 70	30.42 50.17 68.97	101.42 100.35 98.53	0.62 0.82 0.30	100.1 ±0.15	100.20 ± 1.6	0.93(2.31)	1.69(3.97)
FMD	10 50 80	9.89 50.04 80.31	98.94 100.08 100.38	1.14 1.89 1.06	99.80 ±0.76	99.40 ±0.69	0.93(2.31)	1.69(3.97)
QTF	10 20 30	10.00 19.78 29.91	100.08 98.92 99.71	1.15 0.76 0.96	99.57 ±0.59	100.19 ± 0.67	1.45(2.37)	1.61(3.97)
DEX	30 60 70	29.73 59.96 70.03	99.1 99.93 100.04	1.03 0.53 0.35	99.69 ±0.51	99.97 ± 0.42	0.98(2.26)	1.76(4.38)
LVF	30 60 70	30.15 60.20 69.70	100.50 10.34 99.57	1.54 1.30 1.60	100.14 ±0.49	100.08 ±0.50	0.05(2.45)	0.57(9.01)
IRB	25 50 85	25.99 48.90 84.86	99.96 99.80 99.83	1.47 1.33 1.02	99.87 ±0.08	99.99 ±0.07	2.10(2.31)	1.30(5.05)
ITR	100 200 330	100.18 200.20 330.61	100.18 100.10 100.18	1.62 1.87 1.76	99.96 ±0.71	100.38 ±0.72	0.80 (2.45)	1.71 (9.01)

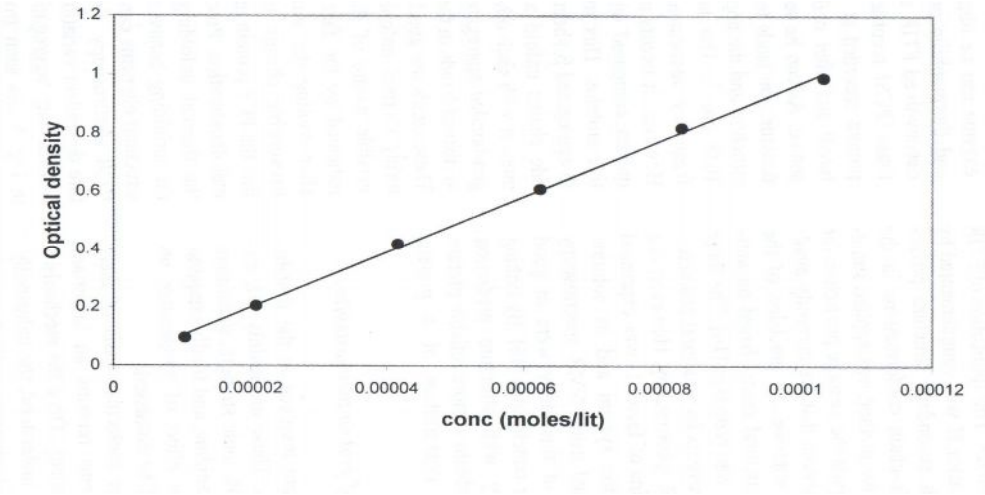


Fig 4 Determination of molar absorption coefficient of DDQ anion

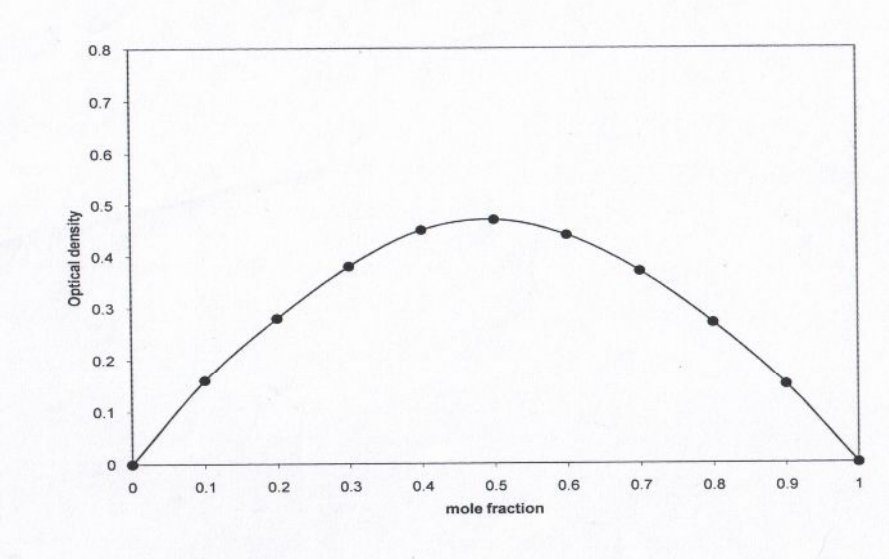


Fig 5 Job's continuous variation plot of DDQ and paroxetine

Many workers used the Benesi - Hildebrand method without fulfilling the condition Do > > Ao and the values of ε obtained varied widely. The ε reported [3, 6] for DDQ : are 9 x 10^3. to 4.17x 10^4.L $mol^{-1}cm.^{-1}$

It is surprising that the molar absorption coefficient of an ion which is expected to be constant and charecteristic of that ion is widely varied. Therefore it is thought worth to determine the molar absorption coefficients of acceptor anions and then use the values to determine the stability constant *K*. To accomplish this, different volumes of dilute solutions of *DDQ wer*e transfered to 25ml standard volumetric flask and excess drug was added and optical density was noted. The addition of drug continued until there is no appreciable increase in the optical density. A plot of d Vs concentration of acceptor gave a straight line from whose slope the molar absorption coefficient of anion of DDQ was determined (Fig 4). This experiment was repeated at least with three drugs and each experiment was repeated three to four times until constant value of molar absorption coefficient (9650 L $mol^{-1}cm^{-1}$) was observed. The stability constant *K*-

$K = (d / \varepsilon) / [(Ao - (d / \varepsilon)] [Do - (d / \varepsilon)]$,

is calculated using the molar extinction coefficient obtained from above experiment.

The stoichiometry of each of the complex has been determined from Job's continous variation method and found to be 1:1 in each case. A typical Job's plot of DDQ with Dextromethorphan is presented in (Fig.5).

Structure activity relation

From the slopes of calibration curves and from formation constants it is clear that the donor abilities of the drugs are in the order : Paroxetine > Famotidine > Quetiapine >Dextromethorphan > Levofloxacin > Irbesartan > Itraconazole.

From the structures of the drugs it is clear that Paroxetine is a 2^o amine hence is expected to show highest basic character which is also in accordance with the slopes of Beer's law plots. Famotidine is a 1^o amine hence stands next to the 2^o amines in the basicity order. Quetiapine, Dextromethorphan, Levofloxacin, Irbesartan and Itraconzole are 3^o amines and are found in the order and their basicities are next to the basicities of 2^o and 1^o .amines. .

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